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1: Curr Opin Microbiol. 2003 Feb;6(1):7-14.

ELSEVIER FULL-TEXT ARTICLE

The various and varying roles of specific chaperones in type III secretion systems.

Parsot C, Hamiaux C, Page AL.

Unite de Pathogenie Microbienne Moleculaire, INSERM U389, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France. cparsot@pasteur.fr

The type III secretion pathway is used by numerous Gram-negative pathogenic bacteria to deliver proteins within the membrane or the cytoplasm of eukaryotic cells with which these bacteria interact. Secretion is regulated by external signals. This requires that, before being secreted, proteins are stored in the cytoplasm where they need to be stabilised, separated from other interaction partners, and maintained in a secretion-competent state. Specialised, energy-independent chaperones play various roles in these functions by associating in the cytoplasm with proteins before their secretion. Some chaperones are also directly involved in modulating transcription in response to secretion.

PMID: 12615213 [PubMed - indexed for MEDLINE]

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1: J Bacteriol. 2000 Apr;182(8):2262-8.

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Complex function for SicA, a Salmonella enterica serovar typhimurium type III secretion-associated chaperone.

Tucker SC, Galan JE.

Section of Microbial Pathogenesis, Boyer Center for Molecular Medicine, Yale School of Medicine, New Haven, Connecticut 06536, USA.

Salmonella enterica encodes a type III secretion system within a pathogenicity island located at centisome 63 that is essential for virulence. All type III secretion systems require the function of a family of low-molecular-weight proteins that aid the secretion process by acting as partitioning factors and/or secretion pilots. One such protein is SicA, which is encoded immediately upstream of the type III secreted proteins SipB and SipC. We found that the absence of SicA results in the degradation of both SipB and SipC. Interestingly, in the absence of SipC, SipB was not only stable but also secreted at wild-type levels in a sicA mutant background, indicating that SicA is not required for SipB secretion. We also found that SicA is capable of binding both SipB and SipC. These results are consistent with a SicA role as a partitioning factor for SipB and SipC, thereby preventing their premature association and degradation. We also found that introduction of a sicA null mutation results in the lack of expression of SopE, another type III-secreted protein. Such an effect was shown to be transcriptional. Introduction of a loss-of-function sipC mutation into the sicA mutant background rescued sopE expression. These results indicate that the effect of sicA on sopE expression is indirect and most likely exerted through a regulatory factor(s) partitioned by SicA from SipC. These studies therefore describe a surprisingly complex function for the Salmonella enterica type III secretion-associated chaperone SicA.

PMID: 10735870 [PubMed - indexed for MEDLINE]

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The putative invasion protein chaperone SicA acts together with InvF to activate the expression of Salmonella typhimurium [Mol Microbiol. 2006]

Salmonella type III secretion-associated protein InvE controls translocation of effector proteins into host cells. [J Bacteriol. 2002]

Salmonella enterica serovar typhimurium-dependent regulation of inducible nitric oxide synthase expression in macrophages by invasins SipB, SipC, and SipD and effector SopB [Infect Immun. 2000]

IpaC from Shigella and SipC from Salmonella possess similar biochemical properties but are functionally distinct [Mol Microbiol. 2001]

InvF is required for expression of genes encoding proteins secreted by the SPI1 type III secretion apparatus in Salmonella typhi [J Bacteriol. 1999]

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1: J Bacteriol. 2005 Sep;187(18):6466-78.

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Analysis of putative Chlamydia trachomatis chaperones Scc2 and Scc3 and their use in the identification of type III secretion substrates.

Fields KA, **Fischer ER**, **Mead DJ**, **Hackstadt T**.

Host-Parasite Interactions Section, Laboratory of Intracellular Parasites, National Institutes of Allergy and Infectious Diseases, Rocky Mountain Laboratories, Hamilton, Montana 59840, USA.

The obligate intracellular pathogen Chlamydia trachomatis expresses a type III secretion system (T3SS) which has the potential to contribute significantly to pathogenesis. Based on a demonstrated role of type III secretion (T3S)-specific chaperones in the secretion of antihost proteins by gram-negative pathogens, we initiated a study of selected putative Chlamydia T3S chaperones in an effort to gain mechanistic insight into the Chlamydia T3SS and to potentially identify Chlamydia-specific secreted products. C. trachomatis Scc2 and Scc3 are homologous to SycD of Yersinia spp. Functional studies of the heterologous Yersinia T3SS indicated that although neither Scc2 nor Scc3 was able to fully complement a sycD null mutant, both have SycD-like characteristics. Both were able to associate with the translocator protein YopD, and Scc3 expression restored limited secretion of YopD in in vitro studies of T3S. CopB (CT578) and CopB2 (CT861) are encoded adjacent to scc2 and scc3, respectively, and have structural similarities with the YopB family of T3S translocators. Either Scc2 or Scc3 coprecipitates with CopB from C. trachomatis extracts. Expression of CopB or CopB2 in Yersinia resulted in their type III-dependent secretion, and localization studies with C. trachomatis-infected cells indicated that both were secreted by Chlamydia.

PMID: 16159780 [PubMed - indexed for MEDLINE]

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Evidence for the secretion of Chlamydia trachomatis CopN by a type III secretion mechanism. [Mol Microbiol. 2000]

The Salmonella enterica serovar typhimurium-encoded type III secretion systems can translocate Chlamydia trachomatis proteins into the cytosol of host cells. [Infect Immun. 2005]

Role of SycD, the chaperone of the Yersinia Yop translocators YopB and YopD. [Mol Microbiol. 1999]

Chlamydia trachomatis type III secretion: evidence for a functional apparatus during early-cycle development. [Mol Microbiol. 2003]

Tetratricopeptide repeats in the type III secretion chaperone, LcrH: their role in substrate binding and secretion. [Mol Microbiol. 2006]

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1: J Bacteriol. 2005 Jan;187(2):473-9.

Interaction between components of the type III secretion system of Chlamydiaceae.

Slepenkin A, de la Maza LM, Peterson EM.

Department of Pathology, Medical Science Building 1, Room D-440, University of California Irvine, Irvine, CA 92697-4800, USA.

Members of the family Chlamydiaceae possess at least 13 genes, distributed throughout the chromosome, that are homologous with genes of known type III secretion systems (TTS). The aim of this study was to use putative TTS proteins of Chlamydophila pneumoniae, whose equivalents in other bacterial TTS function as chaperones, to identify interactions between chlamydial proteins. Using the BacterioMatch Two-Hybrid Vector system (Stratagene, La Jolla, Calif.), lcrH-2 and sycE, positions 1021 and 0325, respectively, from C. pneumoniae CM-1 were used as "bait" to identify target genes (positions 0324, 0705, 0708, 0808 to 0810, 1016 to 1020, and 1022) in close proximity on the chromosome. Interaction between the products of the lcrH-2 (1021) and lcrE (copN) (0324) genes was detected and confirmed by pull-down experiments and enzyme immunoassays using recombinant LcrH-2 and LcrE. As further confirmation of this interaction, the homologous genes from Chlamydia trachomatis, serovar E, and Chlamydophila psittaci, Texas turkey, were also cloned in the two-hybrid system to determine if LcrH-2 and LcrE would interact with their orthologs in other species. Consistent with their genetic relatedness, LcrH-2 from C. pneumoniae interacted with LcrE produced from the three species of Chlamydiaceae; LcrH-2 from C. psittaci reacted with LcrE from C. pneumoniae but not from C. trachomatis; and C. trachomatis LcrH-2 did not react with LcrE from the other two species. Deletions from the N and C termini of LcrE from C. pneumoniae identified the 50 C-terminal amino acids as essential for the interaction with LcrH-2. Thus, it appears that in the Chlamydiaceae TTS, LcrH-2 interacts with LcrE, and therefore it may serve as a chaperone for this protein.

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